

Mini-Review

## THE NEW ADDRESSING PROBLEM IN INTESTINAL CANDIDOSIS

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**Abstract.** *Herein, we discussed a new problem concerning diagnosis, treatment, and monitoring of patients with intestinal candidosis. The lack of official attitude about the significance of Candida overgrowth on intestinal mucosa as well as the absence of guidelines regarding its treatment and required diet, significantly complicate this problem in medical practice. Possible overgrowth of species Saccharomyces cerevisiae-bulardi from probiotics in intestines is a newly recognized problem in diagnostic procedures.*

**Key words:** *intestinal candidosis, Candida overgrowth, Saccharomyces cerevisiae-bulardi.*

### Introduction

The role of *Candida* spp. in the etiology of gastrointestinal disturbances, infection, and diseases hasn't been clarified yet. Gastrointestinal candidosis is still a subject of controversy in scientific circles without a unique opinion about pathogenic potential of this yeast, interpretation of mycological analysis result, and, most importantly, without referral guidelines for its treatment. Lack of official recommendations regarding this problem, alongside a huge number of unreliable theories and misbeliefs in referent literature, electronic media and newspapers, have confused both scientists and laymen since the 1980s [1-3].

### Valid Postulates

We can point out following facts:

- It is well known that *Candida* spp. represent the part of gut microbiota (normal gastrointestinal flora) in healthy people, but in certain cases, these commensal fungi can convert from non-pathogenic to pathogenic ones [4].
- The most important *Candida* infections of the gastrointestinal tract are esophageal and gastrointestinal candidosis in severely immunocompromised. Esophageal candidosis is usually seen in AIDS patients or those receiving long-term chemotherapy. In addition, patients with leukemia and other hematologic malignancies are at increased risk for the development of multiple ulcers on the intestinal mucosa due to fungal in-

fection. Thus, gastrointestinal perforation and complications such as peritonitis or hematogenous spread of fungi to the liver, spleen, and lungs are common in these patients [5].

- A big portion of healthy, immunocompetent, people having *Candida* spp. in their digestive system as part of microbiota, therefore have positive laboratory findings (positive *Candida*-isolates from the stool samples). For this reason, the discrimination between *Candida*-colonization and *Candida*-infection is difficult [6].
- Unlike obligate pathogens, whose detection implies disease, differential diagnosis between *Candida*-infection and *Candida*-colonization is more complex. In order to make a distinction, it is necessary to perform endoscopic biopsy and subsequent histopathological examination. This is the reason why there is still no unique approach regarding the treatment of patients with gastrointestinal candidosis and there are a lot of questionable viewpoints regarding the pathogenic effect of *Candida* on the intestinal mucosa.
- Regardless of many controversial postulates about pathogenic potential of *Candida*, current opinion in medical theory and praxis is that *Candida* spp. has a role in the occurrence of diarrhea after antibiotic consumption. Consequently, nystatin prophylaxis is recommended during the antibacterial treatment [7].
- The theory that immune dysregulation in intestinal mucosa, specifically IgE-mediated reaction to *Candida* antigens, actually leads to local and systemic damage of tissues is under investigation [8].
- There is still no official recommendation for antifungal "intestinal decontamination". However the use of nystatin showed satisfactory anti-*Candida* effect with reduction and even complete withdrawal of symptoms in patients with diarrhea [7, 9].

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## Current Consideration and Observation

The presence of *Candida* yeast as a member of microbiota on intestinal mucosa is mainly benign. However, the results of the newest research concerning *Candida* spp. impact on the digestive tract, demonstrated that, if present, these yeasts may contribute to the destruction of already damaged mucosa. Studies that included patients with gastrointestinal diseases and the ones done on animal models, without a doubt revealed that presence of *Candida* may lead to an even bigger defect and massive inflammation [10-13].

Investigation of Crohn's disease and the presence of *Candida* on intestinal mucosa established the relationship between this inflammatory bowel disease and intestinal *Candida* colonization [10]. Furthermore, it was demonstrated that antifungal treatment to reduce *Candida*-colonization lessens the severity of ulcerative colitis [11]. Moreover, analysis of the animal model suggested that *Candida* colonization may create a vicious cycle where yeasts slow down the healing of inflammatory lesions while inflammation promotes fungal colonization [12]. There is also an assumption that if *Candida* can cause infection and inflammation of the skin, severe damage of nail, inflammation of vulvovaginal mucosa, pseudomembranous and erythematous oral candidosis, as well as perianal eczema, then it can as well have a pathogenic effect at the level of the intestinal mucosa.

## Problems

In addition to these still unresolved issues, in practice, there are also problems of diagnosis and patients treatment. *Candida* spp. can, under the influence of various factors, multiply rapidly and overgrow the rest of gut microbiota, leading to dysbiosis. Based on this simplified, long-standing, concept and on our experience in routine work with patients who have *Candida* infection/colonization of digestive tract, we can point out that physicians usually prescribe local antimycotic, with or without a diet, but recommendation of probiotics is practically mandatory. The role of microorganisms contained inside a probiotic supplement is to successfully colonize intestinal mucosa, stay resistant to the influence of other microorganisms, and persist in intestines. The use of these supplement products increases the possibility of gut colonization with non-pathogenic microbes and preservation of normal balance among usual members of physiologic flora [14]. In the best-case scenario, this treatment will improve condition in a certain number of patients with dysbiosis. However, some of them, despite antifungal treatment, will have recurrent episodes, and will require repeated mycological examination of the stool.

## Our Experience and New Problem

Our previous study [2] as well as the records of approximately 80,000 patients examined in our mycological la-

boratory, showed that in over 60% of cases there are positive findings of *Candida* in the stool samples. Nevertheless, the percentage of patients with *Candida* overgrowth ( $>10^6$  CFU/g of faeces) is significantly lower (8-10%). Interestingly, in a ten-year period, 2% of examined patients had positive findings of yeast overgrowth with causative species being *Saccharomyces (S.) cerevisiae*. This is a ubiquitous ascomycetous yeast that colonizes the respiratory, urinary and gastrointestinal tract of humans and is traditionally considered non-pathogenic. Recently, however, it has started to be considered as a potential pathogen and cause of superficial and invasive fungal infection. Accordingly, *S. cerevisiae* overgrowth on intestinal mucosa could be as problematic as *Candida*-overgrowth. On the other hand, *S. cerevisiae-bulardi* strain is a component of many probiotics and can quickly proliferate during prolonged treatment. In order to correctly interpret the findings of *S. cerevisiae*, we decided to have an interview with 100 patients. All of them, except one, stated that, according to physician recommendation, they have used probiotics that contain *S. cerevisiae-bulardi* strain for more than 20 days.

Besides previously stated problems that there is no general opinion about *Candida*-overgrowth on the intestinal mucosa and official guidelines regarding treatment and diet for this condition are lacking, additional problems are being recognized:

- Mycological analyses of the stool can suggest yeast overgrowth, yet it can be overgrowth of yeast from probiotics.
- In Serbia there are only a few microbiological laboratories equipped for mycological analysis and even fewer for differentiation of yeast strains.
- During the mycological analysis of the stool, overgrowth of *Saccharomyces* yeasts from probiotics can be easily mistaken for high counts of *Candida* spp. Therefore, only in case of macroscopic and microscopic examination, misinterpretation of result as *Candida* overgrowth may occur.
- Errors in result interpretation, as well as the fact that most physicians are neither familiar with the latest trends in mycology, nor with the risk that yeasts from probiotics can lead to *Saccharomyces* overgrowth on the intestinal mucosa, may subsequently mislead the doctor to start „treating the treatment“ [15,16].

To conclude, it would be best to establish laboratory capacity for differentiation between *Candida* and *Saccharomyces* yeast; to implement purposeful education for both medical personnel and laymen which would enable regular patient follow-ups; and before mycological analysis of intestinal microbiota to obtain anamnestic data of each patient regarding disturbance of gastrointestinal tract and consumption of probiotics, as well as the duration of this kind of treatment. Finally, the most correct interpretation of mycological examination can be provided only by a multidisciplinary team and patient participation.

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